12-17-02

AF/1600

DOCKET NO.: ISIS-3070

PATENT

RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1635

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Nielsen, Et Al.

Confirmation No.: 8096

Serial No.: 09/424,521

Group Art Unit: 1635

Filing Date: February 15, 2000

Examiner: James Schultz

For: CONJUGATED PEPTIDE NUCLEIC ACIDS HAVING ENHANCED CELLULAR UPTAKE

EXPRESS MAIL LABEL NO: EV058066408US
DATE OF DEPOSIT: December 16, 2002

EV058066408US

Box ☐ NON-FEE
☒ AF

Assistant Commissioner for Patents
Washington DC 20231

Sir:

REPLY TRANSMITTAL LETTER

Transmitted herewith for filing in the above-identified patent application is:

☐ A Preliminary Amendment.

☒ An Amendment Responsive to the Final Rejection Dated October 17, 2002.

☐ An Amendment Supplemental to the Paper filed .

☐ Other: .

☐ Applicant(s) has previously claimed small entity status under 37 CFR § 1.27.

☐ Applicant(s) by its/their undersigned attorney, claims small entity status under 37 CFR § 1.27 as:

- ☐ an Independent Inventor
- ☐ a Small Business Concern
- ☐ a Nonprofit Organization

☐ This application is no longer entitled to small entity status. It is requested that this be noted in the files of the U.S. Patent and Trademark Office.

☐ Loss of Entitlement Enclosed

☐ Substitute Pages of the Specification are enclosed.

☐ An Abstract is enclosed.

☐ Sheets of Proposed Corrected Drawings are enclosed.

☐ A Certified Copy of each of the following applications: is enclosed.

☐ An Associate Power of Attorney is enclosed.

☐ Information Disclosure Statement.

- ☐ Attached Form 1449.
- ☐ A copy of each reference as listed on the attached Form PTO-1449 is enclosed herewith.

☐ Appended Material as follows: .

☐ Other Material as follows: .

FEE CALCULATION

☒ No Additional Fee is Due.

	REMAINING AFTER AMENDMENT	HIGHEST PAID FOR	EXTRA	SMALL ENTITY RATE	SMALL ENTITY FEE	NOT SMALL ENTITY RATE	NOT SMALL ENTITY FEE
TOTAL CLAIMS	20	(20 MINIMUM) 52	-0-	$9 EACH	$	$18 EACH	$0
INDEP. CLAIMS	5	(3 MINIMUM) 8	0	$42 EACH	$	$84 EACH	$0
FIRST PRESENTATION OF MULTIPLE DEPENDENT				$140	$	$280	$
☐ ONE MONTH EXTENSION OF TIME				$55	$	$110	$
☐ TWO MONTH EXTENSION OF TIME				$200	$	$400	$
☐ THREE MONTH EXTENSION OF TIME				$460	$	$920	$
☐ FOUR MONTH EXTENSION OF TIME				$720	$	$1440	$
☐ FIVE MONTH EXTENSION OF TIME				$980	$	$1960	$
☐ LESS ANY EXTENSION FEE ALREADY PAID				minus	($)	minus	($)
☐ TERMINAL DISCLAIMER				$55	$	$110	$
☐ OTHER FEE OR SURCHARGE AS FOLLOWS:							
TOTAL FEE DUE					$		$0

☐ A check is enclosed in the foregoing amount due.

☐ Petition is hereby made under 37 CFR § 1.136(a) (fees: 37 CFR § 1.17(a)(1)-(4) to extend the time for response to the Office Action of to and through comprising an extension of the shortened statutory period of month(s).

☒ The Commissioner is hereby requested to grant an extension of time for the appropriate length of time, should one be necessary, in connection with this filing or any future filing submitted to the U.S. Patent and Trademark Office in the above-identified application during the pendency of this application. The Commissioner is further authorized to charge any fees related to any such extension of time to Deposit Account 23-3050. This sheet is provided in duplicate.

☒ The Commissioner is authorized to charge payment of the following fees and to refund any overpayment associated with this communication or during the pendency of this application to Deposit Account 23-3050. This sheet is provided in duplicate.

☐ The foregoing amount due for filing this paper.

☒ Any additional filing fees required, including fees for the presentation of extra claims under 37 CFR § 1.16.

☒ Any additional patent application processing fees under 37 CFR § 1.17 or 1.20(d).

SHOULD ANY DEFICIENCIES APPEAR with respect to this application, including deficiencies in payment of fees, missing parts of the application or otherwise, the U.S. Patent and Trademark Office is respectfully requested to promptly notify the undersigned.

Date: December 16, 2002

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ISIS-3070

PATENT

RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1635

#25/K.T. 12/20 RESPONSE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:
Nielsen, et al.

Serial No.: 09/424,521

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Washington, D.C. 20231

REQUEST FOR RECONSIDERATION

This is in response to the Final Rejection mailed on October 17, 2002. Claims 21, 23-27, 31-34, 38-41, 45-48, and 52 are pending. No claims have been amended, canceled or added.

Claims 23, 25-27, and 31 stand rejected under 35 U.S.C. § 102(a) as allegedly anticipated by PCT Patent Application WO/92/20702 ("the 702 Application"). Applicants request reconsideration of this rejection because the 702 Application does not actually describe any claimed invention in a way that would place it in the possession of those skilled in the art. *In re Arkley*, 172 U.S.P.Q. 524, 528 (CCPA 1972) ("The test which determines whether an invention has been anticipated by a reference is whether the description of the invention in the reference is sufficient to put the public in possession of

the invention.") Importantly, the structures recited in claims 23, 24, and 25 do not appear in the 702 Application. Although, the Office Action asserts that "the language of the instant claims allows for merging R_i and R_j into one group that is analogous to the R_i group of structure III of the 702 application, and both may be alkyl groups" (see October 17, 2002 Office Action at page 3), R_i in structure III of the 702 application is H or $-C(O)CH_3$ (see page 10 of the 702 Application) while, in the instant claims, R_i and R_j can be taken together to be alkyl, lipid or steroid. Thus, there is no overlap. For at least this reason, the rejection should be withdrawn.

Even if there was overlap between the generic structure of structure III of the 702 Application and the instant claims, the disclosure of the 702 Application is not such as to put the instant invention in the public's possession. The Office Action alleges that all elements of the instantly claimed compositions are taught by the 702 Application and that selection from an extensive laundry list of substituents is not needed to arrive at the instant claimed compounds. See page 3 of the October 17, 2002 Office Action. However, Applicants note that to arrive at this conclusion, "k" (which is disclosed in the 702 Application as varying between 0 and 5) must be selected as 0, not 1-5, "m" (which is disclosed in the 702 Application as varying between 0 and 5) must be selected as 2, not 0, 1, or 3-5, and "l" (which is disclosed in the 702 Application as varying between 0 and 5) must be selected as 1, not 0 or 2-5. Thus, within these variables alone, a selection of 1 class among 216 possibilities would need to be made. This represents a significant selection that is plainly inconsistent with a finding of anticipation. *Id.* Given the unduly generic nature of the 702 Application's disclosure, the rejection for alleged anticipation is improper and should be withdrawn.

Claims 21, 23-27, 31-34, and 38 stand rejected under 35 U.S.C. § 103 as allegedly being obvious in view of the combined teaching of the 702 Application and Renneisen, *et al*, *Journal of Biological Chemistry*, **1990**, 265, 16337-16342 ("the Renneisen reference"). As discussed above, the 702 Application does not disclose the compounds of the instant invention. There is no allegation that the Renneisen reference cures this defect. As such, the combination of references presented by the Office Action does not produce any claimed invention. For at least this reason, the rejection should be withdrawn.

Claims 39-41, 45-48, and 52 stand rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement with respect to the recited methods. The first paragraph of Section 112, however, requires nothing more than objective enablement. The particular means through which an applicant chooses to enable the practice of his invention, either by the use of illustrative examples or by broad terminology, is of no importance. *In re Marzocchi and Horton*, 169 U.S.P.Q. 367 (C.C.P.A. 1971). In this regard, the instant specification provides considerable disclosure relating to the claimed methods, and there is no evidence of record refuting Applicants' assertion that those skilled in the art would be able to practice the claimed methods to at least some measurable extent. The specification, for example, teaches sites and modes of administration, dose level and administration regimen, and the nature of the pharmaceutical composition (page 15, line 31 to page 18, line 20 of the instant specification). That some experimentation may be required to determine optimum parameters does not preclude enablement and there is no reason to believe that any experimentation attendant to the practice of the claimed invention would be undue. *W. L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 U.S.P.Q. 303, 316 (Fed. Cir. 1983).

Despite Applicants' considerable disclosure, the Office Action makes an unsupported allegation that "several well-known but unsolved problems in the art that persist as obstacles to the practice of the invention" (page 6 of the October 17, 2002 Office Action), For example, although the Office Action asserts that enablement is lacking because the claimed compounds might be inefficiently taken up by cells (*Id.*), because there is no evidence suggesting that the claimed compounds will not be taken up to at least some measurable extent, it is not seen how the potential for inefficient uptake is relevant in assessing enablement of the claimed inventions. Similarly, the mere possibilities presented by the Office Action concerning hybridization within the cell, immune response, and binding to blood proteins are insufficient to sustain a rejection based on lack of enablement.

Finally, the Office Action alleges that Applicants have provided no evidence to rebut the allegations of potential problems associated with therapeutic applications. Applicants contend that such a requirement would wrongly place the burden of persuasion on the Applicant. When rejecting a claim under the enablement requirement,

it is the PTO that bears the initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection is not adequately enabled. *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993). To properly assert a rejection on the grounds that the disclosure is not enabling, the Office Action must provide evidence or sound technical reasoning substantiating its position. Without a reason to doubt the truth of the statements made in the patent application, the application must be considered enabling. *Id.* The following statement from *In re Armbruster*, 512 F.2d 676, 677 (C.C.P.A. 1975) is noteworthy:

> [It] is incumbent upon the Patent Office, whenever a rejection on this basis [lack of enablement] is made, to explain why it doubts the truth or accuracy of any statements in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

As discussed above, no evidence is presented that show that the compositions of the instant claims will not work to at least some measurable extent. Without such a showing, Applicants contend that the Office has not met its initial burden and that the rejection should be withdrawn.

When the present specification is judged in light of the proper test for enablement, it is clear that Applicants have provided extensive teachings as to how to make and how to use the claimed compounds. As such, Applicants respectfully submit that the rejection should be withdrawn.

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. Accordingly, an early and favorable reconsideration of the rejections and an allowance of all of pending claims is earnestly solicited.

Respectfully submitted,

John A. Harrelson, Jr.
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Date: December 16, 2002

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